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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/623,110	07/18/2003	Uri Sagman	4451.003200/RFE	4435

23720 7590 11/19/2007
WILLIAMS, MORGAN & AMERSON
10333 RICHMOND, SUITE 1100
HOUSTON, TX 77042

EXAMINER	
EBRAHIM, NABILA G	

ART UNIT	PAPER NUMBER
1618	

MAIL DATE	DELIVERY MODE
11/19/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/623,110	SAGMAN ET AL.	
	Examiner	Art Unit	
	Nabila G. Ebrahim	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 24 August 2007.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1,3,4,6-10 and 12-19 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1, 3, 4, 6-10, 12-19 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt of Applicant's remarks dated 8/24/07 is acknowledged.

Status of Claims

Claims 1, 3, 4, 6-10, 12-19 are pending in the application.

Status of Office Action: Final.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1,3,4,6-10 and 12-19 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Erlanger et al. US 6593137 (Erlanger) in view of CA Haberzettl, Nanomedicine: destination or Journey? Nanotechnology 13 (2002)

R9–R13 (hereinafter Haberzettl) and further in view of Williams JA et al. (Targeting and therapy of human xenografts in vivo using radiolabeled antibodies.) Int J Radiat Oncol Biol Phys. 1990 Sep;19(3):633-42 (hereinafter "Williams").

Erlanger discloses a therapeutic antibody which is specific for a fullerene or derivative thereof, wherein the fullerene is selected from the group consisting of a fullerene carbon compound having from 20 to 540 carbon atoms, (col. 2, lines 15-18). Erlanger discloses that the possibility of covalent linkage between fullerenes and a specific monoclonal antibody is raised and can be tested (col. 20, lines 4-6), and explains the way of testing the linkage in (col. 20, Lines 18+).

Erlanger used a fullerene specific antibody, however, the reference does not disclose an antibody, which recognizes an antigen.

Haberzettl teaches Buckyballs, fullerenes, nanotubes is the short name for a molecule composed of 60 atoms of carbon arranged in a hollow sphere developing nanobots, successful drug delivery architectures will be enhanced by allowing them to target a particular tissue or organ. The most likely mechanisms to be employed are based on antigen/antibody interactions or binding of target molecules to membrane-bound receptors. Haberzettl discloses that drugs are being encapsulated in a variety of nanoparticles to enhance effectiveness and decrease side effects or to overcome solubility and toxicity issues, these drugs such as nanoparticle-stabilized doxorubicin.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to produce a fullerene tube attached to an

antibody that recognizes an antigen and add a drug such as doxorubicin to enhance the treatment of a disease as disclosed by Haberzettl.

Erlanger and Haberzettl did not disclose the Ab comprising an antigen-binding site selected from the group recited in claim 4.

Williams disclosed radiolabeled antibodies provide a potential basis for selective radiotherapy of human gliomas. Williams used monoclonal antibodies QCI054 and ZME018, which define a tumor-associated and a second melanoma-associated antigen, respectively, demonstrate positive immunoperoxidase staining of the tumor.

Because William disclosed the effectiveness of ZME-018 in treating cancers, it would have been obvious to a man skilled in the art at the time the invention was made to use ZME-018 with fullerene to therapeutically target the cancer site. The expected result would be a composition that comprises a fullerene, an anti-body, which recognizes an antigen, and a radioisotope to be used in a method of treating a cancer.

Instant claim 14 recite the treatment of oxidative stress disease, since Williams include gliomas in his reference, it is recognized that glioma is an oxidative stress disease as evidenced by KL Tsai et al. (Mechanism of oxidative stress-induced intracellular acidosis in rat cerebellar astrocytes and C6 glioma cells), The Journal of Physiology, Vol. 502, Issue 1 161-174, 1997.

The three references did not disclose the doses for using these compounds to treat cancers or oxidative stress syndrome. However, it is within

the skills of an artisan to adjust the dose according to the severity of the condition and the needs of the patient.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to produce a fullerene tube attached to an antibody that recognizes an antigen and add a drug such as doxorubicin to enhance the treatment of a disease as disclosed by Haberzettl, the artisan would be further motivated to use ZME-018 with fullerene to therapeutically target the cancer site because William disclosed the effectiveness of ZME-018 in treating cancers. The expected result would be a composition that comprises a fullerene, an anti-body, which recognizes an antigen, and a radioisotope to be used in a method of treating a cancer or an oxidative stress disease.

3. The prior art made of record is considered pertinent to applicant's disclosure. Laura L. Dugan et al. (Carboxyfullerenes as neuroprotective agents) Proc. Natl. Acad. Sci. USA Vol. 94, pp. 9434-9439, August 1997, Neurobiology. The article discloses that Crboxylic acid C60 derivatives may have attractive therapeutic properties in several acute or chronic neurodegenerative diseases.

Response to Arguments

4. Applicant's arguments filed 8/2/07 have been fully considered but they are not persuasive.

Applicant mainly argues that: Haberzettl's is speculative and hypothetical teachings, ungrounded with any reference to the chemistry of buckyballs, fullerenes, nanotubes, functionalizations thereof, targeting mechanisms,

payloads, and the combination thereof into useful structures, give the person of ordinary skill in the art no motivation to combine Haberzettl with either or both of Erlanger or Williams.

To respond: Applicant claims recite a composition and method of using the composition. The claims does not require a method of making or loading. The prior art disclose the composition as a therapeutic antibody which is specific for a fullerene or derivative thereof, wherein the fullerene a carbon compound having from 20 to 540 carbon atoms, the covalent linkage between fullerenes and a specific monoclonal antibody is raised and can be tested and explains the way of testing the linkage. Haberzettl teaches Buckyballs, fullerenes, nanotubes is a molecule composed of 60 atoms of carbon arranged in a hollow sphere developing nanobots, successful drug delivery architectures will be enhanced by allowing them to target a particular tissue or organ. The most likely mechanisms to be employed are based on antigen/antibody interactions or binding of target molecules to membrane-bound receptors. these drugs such as nanoparticle-stabilized doxorubicin. Note that the document discloses the targeting mechanisms and the payload in the paragraph bridging between the two columns in pages R10 and R11 in a way sufficient to reject the instance claims. For example the document teaches payloading as the simplest payload is a currently available therapeutic agent formulated into a nanoarchitecture. more complex payload would be a functional cell developed as a method of encapsulating hormone producing cells within a nanoarchitecture having well defined and controlled pore size. The reference also discloses Combining

therapeutic agents with targeted nanoparticles, that the payload could be used to enhance or inhibit a physiological or biochemical process and gives examples of the National Cancer Institute that used this combination.

Conclusion

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nabila G. Ebrahim whose telephone number is 571-272-8151. The examiner can normally be reached on 8:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nabila Ebrahim
AU 1618

MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER